

WHAT IS CLAIMED IS:

1. A recombinant HCMV vector comprising a nucleic acid sequence encoding heterologous antigen, wherein the recombinant HCMV vector does not express UL18, UL128, and UL130.
2. The recombinant HCMV vector of claim 1, wherein the recombinant HCMV vector does not express UL146 and UL147.
3. The recombinant HCMV vector of claim 2, wherein the recombinant HCMV vector does not express a UL18 protein, UL128 protein, UL130 protein, UL146 protein, and UL147 protein, or orthologs thereof, due to the presence of one or more mutations in the nucleic acid sequence encoding UL18, UL128, UL130, UL146, and UL147.
4. The recombinant HCMV vector of claim 3, wherein the mutations in the nucleic acid sequence encoding UL18, UL128, UL130, UL146, and UL147 are selected from the group consisting of point mutations, frameshift mutations, truncation mutations, and deletion of all of the nucleic acid sequence encoding the viral protein.
5. The recombinant HCMV vector of any one of claims 1-4, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding UL40, or an ortholog thereof.
6. The recombinant HCMV vector of any one of claims 1-5, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding US28, or an ortholog thereof.
7. The recombinant HCMV vector of any one of claims 1-6, wherein the recombinant HCMV vector does not express UL82 (pp71), or an ortholog thereof.

8. The recombinant HCMV vector of any one of claims 1-7, wherein the recombinant HCMV vector does not express US11, or an ortholog thereof.

9. The recombinant HCMV vector of any one of claims 1-7, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding a microRNA (miRNA) recognition element (MRE), wherein the MRE contains a target site for a miRNA expressed in endothelial cells.

10. The recombinant HCMV vector of claim 9, wherein the miRNA expressed in endothelial cells is miR126, miR-126-3p, miR-130a, miR-210, miR-221/222, miR-378, miR-296, or miR-328.

11. The recombinant HCMV vector of any one of claims 1-8, wherein the recombinant HCMV vector further comprises a nucleic acid sequence encoding a MRE, wherein the MRE contains a target site for a miRNA expressed in myeloid cells.

12. The recombinant HCMV vector of claim 11, wherein the miRNA expressed in myeloid cells is miR-142-3p, miR-223, miR-27a, miR-652, miR-155, miR-146a, miR-132, miR-21, or miR-125.

13. The recombinant HCMV vector of any one of claims 1-12, wherein the heterologous antigen is a pathogen-specific antigen, a tumor antigen, a tissue-specific antigen, or a host self-antigen.

14. The recombinant HCMV vector of claim 13, wherein the pathogen-specific antigen is human immunodeficiency virus (HIV), herpes simplex virus type 1, herpes simplex virus type 2, hepatitis B virus, hepatitis C virus, papillomavirus, *Plasmodium* parasites, or *Mycobacterium tuberculosis*.

15. The recombinant HCMV vector of any one of claims 2-7 and 9-10, wherein the pathogen-specific antigen is an MHC-E supertope.

16. The recombinant HCMV vector of claim 15, wherein pathogen-specific antigen comprises a HIV epitope.

17. The recombinant HCMV vector of claim 16, wherein the HIV epitope is at least 80%, at least 85%, at least 90%, at least 95%, or 100% identical to LDAWEKIRLRPGGKK (SEQ ID NO: 13); DAW EKIRLR (SEQ ID NO: 14); KKAQQAAADTGNSSQ (SEQ ID NO: 15); KAQQAAADT (SEQ ID NO: 16); QMVHQAI SPRTLNAW (SEQ ID NO: 17); HQAI SPRTL (SEQ ID NO: 18); NTMLNTVGGHQAAMQ (SEQ ID NO: 19); VGGHQAAMQ (SEQ ID NO: 20); STLQEQIGWMTNNPP (SEQ ID NO: 21); STLQEQIGW (SEQ ID NO: 22); IVRMYS PVSILDIRQ (SEQ ID NO: 23); RMYSPVSIL (SEQ ID NO: 24); QKQEPIDKELYPLAS (SEQ ID NO: 25); KQEPIDKEL (SEQ ID NO: 26); SFSFPQITLWQRPLV (SEQ ID NO: 27); VRQYDQILIEICGKK (SEQ ID NO: 28); EPFRKQNPDIYIYQL (SEQ ID NO: 29); YVDGAANRETKLGKA (SEQ ID NO: 30); EEHEKYSNWRAMAS (SEQ ID NO: 31); or ILDLWVYHTQGYFPD (SEQ ID NO: 32).

18. The recombinant HCMV vector of claim 13, wherein the tumor antigen is related to acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, acute lymphoblastic leukemia, chronic lymphoblastic leukemia, non-Hodgkin's lymphoma, multiple myeloma, malignant melanoma, breast cancer, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer, colon cancer, renal cell carcinoma (RCC), or germ cell tumors.

19. The recombinant HCMV vector of claim 13, wherein the host self-antigen is an antigen derived from the variable region of a T cell receptor (TCR) or an antigen derived from the variable region of a B cell receptor.

20. A pharmaceutical composition comprising the recombinant HCMV vector of any one of claims 1-19 and a pharmaceutically acceptable carrier.

21. An immunogenic composition comprising the recombinant HCMV vector of any one of claims 1-19 and a pharmaceutically acceptable carrier.

22. Use of the recombinant HCMV vector of any one of claims 1-19 in the manufacture of a medicament for use in generating an immune response in a subject.

23. The recombinant HCMV vector of any of claims 1-19 for use in generating an immune response in a subject.

24. Use of the recombinant HCMV vector of claim 13 or claim 18 in the manufacture of a medicament for use in treating or preventing cancer in a subject.

25. The recombinant HCMV vector of claim 13 or claim 18 for use in treating or preventing cancer in a subject.

26. Use of the recombinant HCMV vector of any one of claims 13-17 in the manufacture of a medicament for use in treating or preventing a pathogenic infection in a subject.

27. The recombinant HCMV vector of any one of claims 13-17 for use in treating or preventing a pathogenic infection in a subject.

28. Use of the recombinant HCMV vector of claim 13 or claim 19 in the manufacture of a medicament for use in treating an autoimmune disease or disorder in a subject.

29. The recombinant HCMV vector of claim 13 or claim 19 for use in treating an autoimmune disease or disorder in a subject.

30. The CMV vector for use, or use in manufacture, of any one of claims 22-29, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-E or an ortholog thereof.

31. The CMV vector for use, or use in manufacture, of any one of claims 22-29, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60% or at least 75% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-II or an ortholog thereof.

32. The CMV vector for use, or use in manufacture, of any one of claims 22-29, wherein fewer than 10%, fewer than 20%, fewer than 30%, fewer than 40%, or fewer than 50% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-class Ia or an ortholog thereof.

33. The CMV vector for use, or use in manufacture of any one of claims 22-29, wherein at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the CD8+ T cells elicited by the recombinant HCMV vector are restricted by MHC-class Ia or an ortholog thereof.

34. A method of generating CD8+ T cells that recognize MHC-E-peptide complexes, the method comprising:

- a. identifying a first CD8+ TCR from a set of CD8+ T cells, wherein the set of CD8+ T cells are generated from the recombinant HCMV vector of any one of claims 2-7, 9, 10, 13, or 14, wherein the first CD8+ TCR recognizes a MHC-E/heterologous antigen-derived peptide complex;
- b. isolating one or more CD8+ T cells from a second subject; and
- c. transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter

operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more TCR-transgenic CD8+ T cells that recognize MHC-E-peptide complexes.

35. A method of generating CD8+ T cells that recognize MHC-II-peptide complexes, the method comprising:

- a. identifying a first CD8+ TCR that recognizes a MHC-II/heterologous antigen-derived peptide complex from a set of CD8+ T cells that recognize MHC-II/peptide complexes, wherein the set of CD8+ T cells are generated from the recombinant HCMV vector of any one of claims 1-8, 11, or 12;
- b. isolating one or more CD8+ T cells from a second subject; and
- c. transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more CD8+ T cells that recognize a MHC-II peptide complexes.

36. A method of generating CD8+ T cells that recognize MHC-I-peptide complexes, the method comprising:

- a. identifying a first CD8+ TCR that recognizes a MHC-I/heterologous antigen-derived peptide complex from a set of CD8+ T cells that recognize a MHC-I/heterologous antigen-derived peptide complex, wherein the set of CD8+ T cells are generated from the recombinant HCMV vector of any one of claims 1-8;
- b. isolating one or more CD8+ T cells from a second subject; and
- c. transfecting the one or more CD8+ T cells with an expression vector, wherein the expression vector comprises a nucleic acid sequence encoding a second CD8+ TCR and a promoter operably linked to the nucleic acid sequence encoding the second CD8+ TCR, wherein the second

CD8+ TCR comprises CDR3 α and CDR3 β of the first CD8+ TCR, thereby generating one or more CD8+ T cells that recognize MHC-I peptide complexes.

37. A recombinant HCMV vector comprising a nucleic acid encoding one or more human immunodeficiency virus antigens, wherein the human immunodeficiency virus antigen is between 9 and 15 amino acids in length and that is at least 90%, at least 95%, or 100% identical to the amino acid sequence of LDAWEKIRLRPGGKK (SEQ ID NO: 13); DAWEKIRLR (SEQ ID NO: 14); KKAQQAAADTGNSSQ (SEQ ID NO: 15); KAQQAAADT (SEQ ID NO: 16); QMVHQAI SPRTLNAW (SEQ ID NO: 17); HQAI SPRTL (SEQ ID NO: 18); NTMLNTVGGHQAAMQ (SEQ ID NO: 19); VGGHQAAMQ (SEQ ID NO: 20); STLQEQIGWMTNNPP (SEQ ID NO: 21); STLQEQIGW (SEQ ID NO: 22); IVRMYSPVSILDIRQ (SEQ ID NO: 23); RMYSPVSIL (SEQ ID NO: 24); QKQEPIDKELYPLAS (SEQ ID NO: 25); KQEPIDKEL (SEQ ID NO: 26); SFSFPQITLWQRPLV (SEQ ID NO: 27); VRQYDQILIEICGKK (SEQ ID NO: 28); EPFRKQNPDIVIYQL (SEQ ID NO: 29); YVDGAANRETKLGKA (SEQ ID NO: 30); EEHEKYSNWRAMAS (SEQ ID NO: 31); or ILDLWVYHTQGYFPD (SEQ ID NO: 32).